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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,406	09/01/2000	Jennifer L. West	RICE 100	7133

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[REDACTED] EXAMINER

DI NOLA BARON, LILIANA

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1615

DATE MAILED: 12/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/653,406	WEST ET AL.	
	<b>Examiner</b> Liliana Di Nola-Baron	<b>Art Unit</b> 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 14 March 2002.
- 2a) This action is **FINAL**.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-23 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>13</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)                 |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

This supplemental action is sent in response to Applicant's statement, confirming that the final rejection mailed on May 7, 2002 was not received by the Applicant.

Receipt of Applicant's amendment, filed on March 14, 2002, is acknowledged.

### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claim 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ragheb et al. or Keefer et al. in view of Hubbell et al. or Igo et al. in view of Hubbell et al.

The claimed invention refers to a macromer composition comprising a NO carrying region or NO modulating compound, a method of making said composition and methods comprising administering said composition.

Ragheb et al. provides a medical device comprising a porous layer composed of a polymer, which controls the delivery of a bioactive agent, teaches that the biocompatible polymers may be applied by vapor deposition and polymerize upon condensation from the vapor phase or may be photolytically polymerizable, and includes vasodilators among the bioactive materials used in the invention (See e.g., col. 3, line 4 to col. 5, line 10 and col. 8, lines 51-63). Ragheb et al. includes

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polymers derived from photopolymerizable monomers, such as monomers having two crosslinkable double bonds and bioabsorbable polymers, such as poly(L-lactic acid), polycaprolactone and PEO/PLA, among the polymer systems used in the invention (See e.g., col. 11, line 25 to col. 12, line 32). Ragheb et al. teaches that the invention provides an implantable medical device, which achieves precise control over the release of one or more bioactive materials contained in the device, and is particularly useful in preventing restenosis (See e.g., col. 25, lines 20-50).

Keefer et al. discloses a method comprising administering a NO-releasing agent and teaches that the NO-releasing agent can be a polymer, to which is bound a NO-releasing agent (See e.g., col. 4, lines 20-44). Keefer et al. teaches that the polymer enables the controllable and predictable release of NO (See e.g., col. 5, line 19 to col. 6, line 5). Keefer et al. teaches that any polymer can be used for the invention, including polyolefins, polyethers, polyamides, dendrimers and biopolymers, and the NO-releasing agents can be administered in a variety of forms, including microparticles and patches (See e.g., col. 9, line 32 to col. 10, line 8).

Keefer et al. does not specify the various regions of the monomers in the polymer.

Hubbell et al. discloses multifunctional polymers for use in inhibiting cell adhesion, said polymers including biocompatible polymers, such as PVP, PVA, poly(amino acids) and copolymers of the monomers thereof, and polysaccharides (See e.g., col. 2, line 40 to col. 3, line 40). In particular, Hubbell et al. teaches that when the poly(B) in the block copolymer is not sufficiently water-soluble, it can be brought into solution by grafting with water-soluble poly(A),

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which includes polyethylene oxide, PVP, PVA, polysaccharides, such as dextran and cellulose, polyacrylates and polyacrylamides (See e.g., col. 3, lines 9-40). Hubbell et al. teaches that PEG may be used as an initiator for the polymerization of a polyamino acid and ethylene oxide polymerization is initiated by addition of poly (L-lysine) (See e.g., col. 12, lines 9-33). Hubbell et al. teaches the polymers of the invention can be used for medical applications to deliver bioactive compounds and for the prevention of thrombus formation (See e.g., col. 13, line 58 to col. 14, line 5). Hubbell et al. teaches that thrombosis can be blocked using bifunctional polymers, such as PVP-chitosan, or PEG-PVA block copolymers (See e.g., col. 15, line 52 to col. 16, line 37). Hubbell et al. teaches that polymers exhibiting more than one manner of degradation are required in some cases to achieve different results (See e.g., col. 16, lines 44-50).

Igo et al. provides treatment of thrombosis and restenosis, comprising administration of a nitrovasodilator, including NO and NO donor agents (See e.g., col. 6, line 59 to col. 7, line 37). Igo et al. teaches that the method of administration includes an implant capable of controlled-release of the bioactive agent, and preferably the implant comprises a biodegradable polymer (See e.g., col. 10, lines 39-65). Igo et al. teaches that therapeutic substances can be administered by using the apparatus of the invention (See e.g., col. 13, lines 54-67). Igo et al. does not specify the various regions of the monomers in the polymer.

Hubbell et al. discloses multifunctional polymers for use in inhibiting cell adhesion, said polymers including biocompatible polymers, such as PVP, PVA, poly(amino acids) and copolymers of the monomers thereof, and polysaccharides (See e.g., col. 2, line 40 to col. 3, line

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40). In particular, Hubbell et al. teaches that when the poly(B) in the block copolymer is not sufficiently water-soluble, it can be brought into solution by grafting with water-soluble poly(A), which includes polyethylene oxide, PVP, PVA, polysaccharides, such as dextran and cellulose, polyacrylates and polyacrylamides (See e.g., col. 3, lines 9-40). Hubbell et al. teaches that PEG may be used as an initiator for the polymerization of a polyamino acid and ethylene oxide polymerization is initiated by addition of poly (L-lysine) (See e.g., col. 12, lines 9-33). Hubbell et al. teaches the polymers of the invention can be used for medical applications to deliver bioactive compounds and for the prevention of thrombus formation (See e.g., col. 13, line 58 to col. 14, line 5). Hubbell et al. teaches that thrombosis can be blocked using bifunctional polymers, such as PVP-chitosan, or PEG-PVA block copolymers (See e.g., col. 15, line 52 to col. 16, line 37). Hubbell et al. teaches that polymers exhibiting more than one manner of degradation are required in some cases to achieve different results (See e.g., col. 16, lines 44-50).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply the teachings of Ragheb et al. or modify the polymers comprising the nitrovasodilator disclosed by Keefer et al. or Igo et al., by including multifunctional organic polymers, as taught by Hubbell et al., to optimize the release of the bioactive agents. Because of the teachings of Hubbell et al., that sparingly water-soluble polymers can be grafted with water-soluble polymers, and in some cases polymers exhibiting more than one manner of degradation are required to ensure controlled release of a bioactive agent, one of ordinary skill in the art would have a reasonable expectation that the compositions and methods claimed in the instant

application would be successful. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

3. Applicant's arguments filed on March 14, 2002, have been fully considered but they are not persuasive.

4. Applicant's amendment has overcome the 35 U.S.C. 112, second paragraph rejection of claim 2 of the previous Office action. Accordingly, that rejection is withdrawn.

5. Applicant argues that the prior art does not teach the delivery of a bioactive agent bound to a polymerizable macromer. In response to said argument, it is noted that Hubbell et al. teaches that polymers, such as polyamines, polyethylene oxide, PVP, PVA, polysaccharides, such as dextran and cellulose, polyacrylates and polyacrylamides, which are taught in the prior art as being bound to a NO-releasing agent, can be further polymerized (See e.g., col. 3). Furthermore, Applicant's attention is drawn to U.S. Patent 6,262,206B1 to Nesvadba et al., which teaches that polymerization can be started and stopped at will and it is possible to carry out additional polymerizations with the same or different monomers to prepare multi-block copolymers (See e.g., col. 13, lines 4-26). It is also noted that Applicant uses language, which is not limited to the scope of the claims. A review of the specification indicates that Applicant recognizes a macromer as a copolymer produced from the reaction of polyethylene glycol N-hydroxysuccinimide monoacrylate with L-cysteine (See Example 1). Therefore, it appears that Applicant recognizes a macromer as a copolymer, so the scope of the claims permits polymers

and Applicant's argument that the polymers disclosed in the prior art are not polymerizable is not persuasive.

***Conclusion***

6. Claims 1-23 stand rejected.
7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

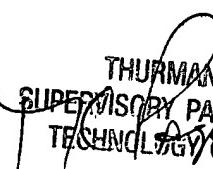
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

December 18, 2002

  
THURMAN K. PAGE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600